

RADIOBIOLOGICAL STUDIES AT LRRI USING MICROGRAY TO MILLIGRAY GAMMA-RAY DOSES

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A key focus of the Department of Energy's Low Dose Radiation Research Program is on understanding the importance of radiation adaptive responses in humans after exposure to low linear-energy-transfer (LET) radiation doses ≤ 100 mGy (10 rad). Our research focuses on elucidating the biological bases for radiation adaptive responses in the lung for the indicated dose range and for suppressing lung cancer. Research was initiated around October 1, 2009; thus, only limited experimental research has been conducted at this time. Our initial research has in part focused on characterizing the radiation field associated with use of a Gammacell 1000 Unit (Atomic Energy of Canada Limited), which was designed to deliver large radiation doses to relatively small biological targets. We have also been developing strategies for delivering radiation doses (≤ 100 mGy) to human bronchial epithelial cells (HBEC) in culture and to mice.

Initial radiation field characterization involved mapping the spatial distribution of the gamma-ray dose rate over the central region of the exposure chamber when minimal within-unit biological shielding is employed. The biological shielding is achieved with built-in steel-encapsulated lead which can be rotated relative to the radiation source. The absorbed dose rate (free-in-air) distribution for a fixed exposure time was measured in water-equivalent medium (polystyrene) using radiochromic film. The free-in-air adsorbed dose rate distribution was evaluated over a vertical plane through the axis of the rotation field of the unit's rotator. Dose rates varied both horizontally and vertically with the lowest dose rates at the bottom of the exposure chamber.

We also evaluated radiation dose gradients over medium-free, 60-mm cell-culture plates in the center of the exposure chamber at different heights from the bottom using nanoDot dosimeters (Landauer, Inc., Glenwood, IL) when minimum exposure time and maximum within-unit biological shielding was used. The nanoDot dosimeter is a new innovation for single-point radiation measurement that uses Optically Stimulated Luminescence (OSL) technology. Reader calibrations were made for cesium-137, which is the source used in our Gammacell 1000 Unit. The nanoDot detection limit is 50 μ Gy. Modest variation in radiation absorbed dose was recorded vertically for rotating samples and a significant horizontal dose gradient (over Petri dishes) was found when no rotation was used. The gradient relates to the incident beam being horizontal. The lowest dose was at the bottom of the chamber as expected based on field-mapping results indicated above.

We have also employed nanoDot dosimeters in mouse phantoms (3 carcasses oriented vertically within 50-mL polypropylene centrifuge tubes placed inside a lidded stainless steel canister with lead foil layers inside for additional shielding). Phantom sizes were selected to be representative of the mice to be used in our future studies. Thoracic and abdominal region absorbed doses were recorded for rotating mouse phantoms as well as free-in-air doses at the surface of the housing tube at the thoracic level for 6- and 60-s exposures. Dose rates recorded with nanoDot dosimeters were similar for all three sites and for both exposure times but were more variable for the 6-s exposures as expected.

We were able to routinely get reasonably reproducible gamma radiation absorbed doses in the range of interest (e.g., ≤ 100 mGy) both for cell culture plates (without extra lead foil shielding)

and mouse phantoms (with extra lead foil shielding). The minimum in-chamber dose (cell culture plate midline) within the exposure unit when turned on and with maximal within-unit shielding was approximately 30 mGy delivered in 6 seconds (minimum exposure time for unit automatic shutdown) without extra lead foil shielding. Similar doses were obtained for mouse phantoms. In addition, we have taken advantage of the unit's leakage radiation when the unit is turned off (i.e., leakage radiation through the biological shield). Leakage dose rates (corrected for natural background using transient and location dosimeters) were evaluated at the center of cell-culture plates placed at three select locations on the top of the unit indicated as Positions A, B, and C. Resultant calibration curves are presented in Figure 1 and demonstrate our ability to deliver ultra low radiation doses (< 10 microgray) from a gamma-ray unit intended to deliver large doses to biological specimens.

We have just initiated a pilot adaptive-response study using normal and transformed HBEC and dose \geq 30 mGy with or without additional exposure to the benzo(a)pyrene (BaP) related metabolite BDPE. We are also examining the effect of dose \geq 30 mGy on cytokine secretion from macrophages and lung fibroblast. We will report our preliminary findings at the workshop. Animal studies to be initiated this year are being planned and will focus on using small gamma-ray doses to prevent lung cancer induction by injected BaP in lung-cancer-prone A/J mice.

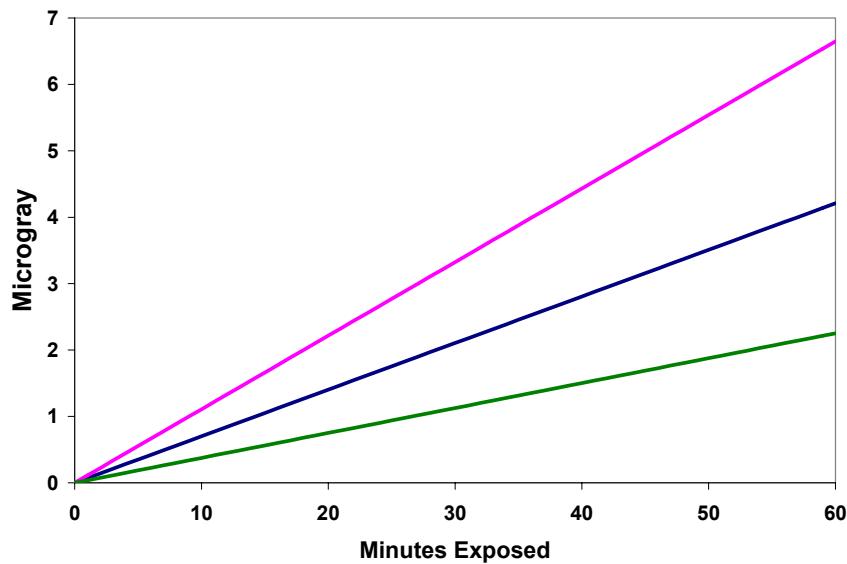


Figure 1. Calibration curves for positions B (upper line), A (middle line), and C (lower line) on the surface of the Gammacell 1000 Unit. The results are based on extrapolations from 87.5 h exposure data.

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